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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,836	10/04/1999	CARL GUSTAV FIGDOR	2578-4230US	8137

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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/214,836	FIGDOR ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,11,15,19,21,24 and 30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,11,15,19,21,24 and 30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040329*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed March 4, 2004 is acknowledged and has been entered. Claims 2, 14, 20, 22, and 25 have been canceled. Claims 4, 11, 19, 21, and 24 have been amended. Claim 30 has been added.

2. Claims 4, 11, 15, 19, 21, 24, and 30 are pending in the application and are currently under prosecution.

Priority

3. Applicant has met the requirements set forth under 35 U.S.C. § 119(a)-(d) to receive the claimed benefit of the earlier filing date of EP 96201945.1.

Information Disclosure Statement

4. The information disclosure filed March 29, 2004 has been considered. An initialed copy is enclosed.

Grounds of Objection and Rejection Withdrawn

5. Unless specifically reiterated below, Applicant's amendments to the claims has obviated or rendered moot the grounds of rejection set forth in the previous Office action mailed November 4, 2003.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 4, 21, and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons stated in section 8 of the previous Office Action mailed November 4, 2003.

At page 5 of the amendment filed March 4, 2004, Applicant has stated that at the Examiner's recommendation, Applicant has amended claims 21 and 24 so that the claims are drawn to more broadly to "an immunogenic composition", as opposed to "a vaccine". Although at page 4 of the previous Office action, the Examiner stated amending claims 21 and 24 to recite, for example, an immunogenic composition, rather than a vaccine, can obviate the grounds of rejection of the claims under 35 USC § 112, first paragraph, as lacking a sufficiently enabling disclosure, the Examiner expresses regret that upon further consideration of the merit of Applicant's disclosure and the record as a whole, the disclosure still fails to meet the enablement requirement for the following reasons:

Claim 21 and 24 are drawn to an "immunogenic composition" comprising the peptide of claim 4. Claim 4 is drawn to a peptide "being immunogenic with lymphocytes directed against metastatic melanoma". The claimed invention, i.e., an immunogenic composition comprising a peptide that is immunogenic with lymphocytes directed against metastatic melanoma is only asserted by the specification to be useful as a vaccine in treating and preventing cancer. For clarity, while claim 11 uses a peptide comprising SEQ DI NO: 4, claim 11 does not recite that the peptide is immunogenic, but merely that it be capable of reacting (i.e., binding) to tumor infiltrating lymphocytes with increased affinity relative to the peptide of SEQ ID NO: 9. Furthermore, while claim 30 is drawn to a peptide comprising the amino acid sequence of SEQ ID NO: 1, the peptide is not necessarily immunogenic. In contrast, since the rejected claims recite the subject matter must be capable of eliciting a lymphocyte-mediated immune response against melanoma, according to the disclosure, the claimed invention

has no other use, apart from as a component of a vaccine to treat and prevent cancer. Therefore, for the reasons already of record, whether the invention be claimed as a vaccine or an immunogenic composition, the disclosure would not be sufficient to enable the skilled artisan to use the claimed invention without the need to perform an undue amount of additional experimentation.

In addition, as Applicant has remarked claims 21 and 24 presently are more broadly drawn to an immunogenic composition, as opposed to a vaccine. The specification, however, only teaches the use of the claimed immunogenic composition as a vaccine; the specification does not teach any other use for the claimed invention. Therefore, since the claimed invention cannot be used as a vaccine by the skilled artisan without having to first perform an undue amount of additional experimentation, then the artisan have to discover another use for claimed invention, if the invention were to be useful. The need to discover an undisclosed use for the claimed invention would amount to a need to perform an undue amount of experimentation.

Accordingly, while the Examiner again expresses regret for misleading Applicant by suggesting that this rejection can be overcome by amending the claims to recite "an immunogenic composition", as opposed to "a vaccine", the grounds of rejection set forth previously are herein maintained.

8. Claims 4, 11, 15, 19, 21, and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection.

Claims 4, 11, 15, and 19 recites the limitation, "wherein said peptide has an increased binding affinity towards [...] *HLA-A*0201 expressing lymphocytes*" (italicized for emphasis). At page 25, paragraph 2, for example, the specification provides written support for the limitation, "wherein said peptide has an increased

binding affinity towards HLA-A*0201; however, the specification, including the claims, as originally filed, does not appear to provide proper and sufficient written support for a peptide that has increased binding affinity towards "HLA-A*0201 expressing lymphocytes". Accordingly, the term appears to introduce new matter and thereby violates the written description requirement set forth under 35 USC § 112, first paragraph.

Claims 21 and 24 recite "an immunogenic composition". Although the previous Office action suggested amending claims 21 and 24 to recite, for example, "an immunogenic composition" comprising the peptide of claim 4, rather than "a vaccine", as a means to obviate the above enablement rejection of claims 21 and 24, the specification, including the claims, as originally filed does not appear to provide proper and sufficient written support for the broader term, "an immunogenic composition". Accordingly, the term appears to introduce new matter and thereby violates the written description requirement set forth under 35 USC § 112, first paragraph.

These issues might be resolved if Applicant were to point to particular disclosures in the specification that are believed to provide the necessary written support.

9. Claims 30 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 30 is drawn to a peptide comprising the amino acid sequence of SEQ ID NO: 1. At page 5 the specification discloses the term "peptide" is not restricted to a protein of any particular length. Accordingly, the claim is drawn to a genus of peptides or proteins comprising SEQ ID NO: 1, which are widely variant in both structure and function.

The specification describes SEQ ID NO: 1 as a short 9 amino acid sequence. The sequence is not apparently associated with any particular

secondary or tertiary structure; nor is it associated with any particular functional attribute of an intact peptide or protein comprising the amino acid sequence. Therefore, SEQ ID NO: 1 is not deemed representative of, or sufficiently descriptive of at least a substantial number of the members of the claimed genus of peptides and proteins comprising the sequence. Moreover, even given benefit of Applicant's disclosure, the skilled artisan could not immediately recognize, envision, or distinguish at least a substantial number of the members of the claimed genus, so the disclosure would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing

distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

10. Claim 30 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making and using a peptide consisting of SEQ ID NO: 1, or conjugate thereof and a radionuclide, for isolating melanoma antigen reactive tumor infiltrating lymphocytes according to the method of claim 11, does not reasonably provide enablement for making the peptide of claim 30. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 30 is drawn to a large genus of peptide and proteins comprising SEQ ID NO: 1. The members of the claimed genus are expected to vary widely in structure and function.

Factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). These factors include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

Apart from the peptide consisting of SEQ ID NO: 1, the specification has not described any other peptide or protein comprising SEQ ID NO: 1. The specification cannot enable the skilled artisan to make what has not been described.

Furthermore, the specification cannot teach one to use what has not been described, particularly since the art is so highly unpredictable. Skolnick et al. (*Trends in Biotechnology* **18**: 34-39, 2000) discloses that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2). Thus, one skilled in the art would not accept the assertion, which is based only upon an observed similarity in amino acid sequence, i.e., the commonality of SEQ ID NO: 1, that a polypeptide comprising SEQ ID NO: 1 could be used, for example, to isolate melanoma antigen reactive tumor infiltrating lymphocytes, simply because a peptide consisting of SEQ ID NO: 1 can be so used.

Conclusion

11. No claims are allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

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June 14, 2004

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